Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 85-87 are pending in the application, with claim 85 being the independent claim. Claims 88-100 have been withdrawn from consideration. Claim 85 has been amended to recite that the analogs are produced by molecular biological means as required by the Examiner. Support for this amendment can be found throughout the specification, *inter alia*, the Examples. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 85-87 are rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to comply with the written description requirement. Not in acquiescence to the propriety of the rejection, but rather solely to advance prosecution, Applicants have amended claim 85 to recite that the analog is made by molecular biological means. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

The Examiner also alleges that the claims do not comply with the written description requirement because they encompass mutant molecules that are not disclosed in the application. To satisfy the written description requirement of 35 U.S.C. § 112,

first paragraph, an Applicant must convey with reasonable clarity to those skilled in the art that, as of the effective filing date, the Applicant was in possession of the invention. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1560, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991).

The Federal Circuit has recently adopted the standard for determining compliance with the written description requirement as set forth in the USPTO's "Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, Written Description Requirement." *See Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). According to the USPTO's Guidelines:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics.

MPEP § 2163; *See also, Enzo*, 296 F.3d at 1324, 63 USPQ2d at 1613.

Applicants respectfully assert that a person of ordinary skill in the art, upon reading the specification, would conclude that, as of the effective filing date, Applicants had invented the claimed subject matter. The specification describes and illustrates several analogs of two model proteins, ubiquitin and TNFα (*see, e.g.* Examples 1-3). The specification further describes methods to make and also test the analogs for their ability to generate autoantibodies *in vivo* (*see, e.g.* Examples 3-9). Therefore, not only does the specification teach making analogs of self-proteins, but also discloses methods to test the analogs for the asserted activity. Therefore, Applicants respectfully assert that

the claims do satisfy the written description requirement. Accordingly, Applicants request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 85-87 are rejected under 35 U.S.C. § 112 as allegedly indefinite. Applicants respectfully traverse the rejection.

Claim 85 is rejected because the phrase "the tertiary structure of the pathogenic self-protein is essentially preserved" is allegedly unclear. Applicants respectfully assert that those of skill in the art recognize that antibodies are raised against conformational (three dimensional) epitopes. Therefore, in order to raise autoantibodies against the pathogenic self-proteins, the tertiary, or three dimensional, structure of the self-protein must be maintained. Accordingly, Applicants respectfully assert that the phrase is definite and respectfully request that the rejection be reconsidered and withdrawn.

Claim 86 is rejected because the phrase "preserve flanking regions" is allegedly unclear. Applicants respectfully assert that those of skill in the art recognize that the flanking regions on either side of an epitope could be important in maintaining the tertiary structure of the analog. As explained above, antibodies are raised against conformational (three dimensional) epitopes. Therefore, one of ordinary skill in the art would recognize that flanking regions may need to be maintained in order to raise autoantibodies against the pathogenic self-proteins. Accordingly, Applicants respectfully assert that the phrase is definite and respectfully request that the rejection be reconsidered and withdrawn.

Claim 85 is also rejected because the phrase "pathogenic self-protein" is allegedly unclear. Applicants respectfully assert that those of skill in the art recognize that a pathogenic self-protein is a self-protein that causes or is capable of causing disease. Every nuance of the claims does not have to be explicitly described in the specification. *See, e.g., Vas-Cath, Inc. v Mahurkar*, 935 F.2d 1555 at 1563 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972) (stating "the description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient"). MPEP §2163. Therefore, Applicants assert that the phrase "pathogenic self-proetin" is definite. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 102

Claims 85 and 86 are rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Russell-Jones *et al.* (WO 92/05192), as evidenced by Dean *et al.* (U.S. Pat. No. 5,716,596). Applicants respectfully traverse the rejection.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987); *see also* MPEP § 2131. The Examiner asserts that Russell-Jones teaches that, through the use of recombinant DNA technology, the TraT peptide can be inserted into an immunogen via substituting the TraT peptide for a peptide contained in the immunogen. Office Action, paragraph 11. However, closer inspection of the cited passages by the Examiner (pages 31-32) reveals that Russell-Jones does not disclose an analog of a *self-protein*, but rather

replacement of so called "suppressor regions" in "otherwise immunogenic molecules" such as HIV gp120. The use of "otherwise immunogenic proteins" in Russell-Jones is also supported by the disclosure on page 8, line 36 through page 9, line 3 which states, in relevant part, "[T]ypically, the at least one "immunogen" will be a molecule which is poorly immunogenic, but immunogenic molecules are not excluded." The claimed invention is directed to substituting existing regions of self-proteins so that an immune response is generated because the original, self-proteins are not immunogenic at all.

In addition, contrary to the assertion by the Examiner, somatostatin is not a pathogenic self-protein. As evidenced by Dean, somatostatin is a tetradecapeptide which, in native configuration, is of limited use. (Dean, col. 1, lines 20-41). Also, as a tetradecapeptide, one could not substitute one or more fragments of somatostatin with a foreign T cell epitope such that the structure of the protein is essentially preserved.

Therefore, since Russell-Jones, even as evidence by Dean, does not disclose substitutions of self-proteins such that the tertiary structure is essentially preserved, it does not teach each and every element of the claims. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejections under 35 U.S.C. § 103

Claims 85-87 are rejected under 35 U.S.C. § 103 as allegedly unpatentable over Russell-Jones (of record) in view of Dean (of record). Applicants respectfully traverse the rejection.

In order to establish a *prima facie* case of obviousness, the proper analysis is to first consider whether the following three criteria are met: (1) there must be some reason,

either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP § 2143. "[I]n formulating a rejection under 35 U.S.C. § 103(a) based upon a combination of prior art elements, it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." Memorandum from the United Patent and Trademark Office, "Supreme Court decision on *KSR Int'l. Co. v. Teleflex Inc.*," (May 3, 2007) at page 2. Applicants respectfully assert that the Examiner has not provided an adequate reason to combine the reference teachings and arrive at Applicants' claimed invention, and thus the first criteria necessary to establish a *prima facie* case of obviousness has not been met.

As described above, Russell-Jones describes the identification of T cell epitopes from the TraT protein and further their use in enhancing immune responses to immunogens. Russell-Jones does not disclose generation of an analog of a *self-protein*, but at best, replacement of so called "suppressor regions" in "otherwise immunogenic molecules" such as HIV gp120. The deficiencies of Russell-Jones are not cured by Dean. Dean discloses *radiolabeled* somatostatin-derived peptides and their use in imaging and therapy.

As amended, the claims are directed to administering an analog of a self-protein made by molecular biological means, to induce autoantibodies in a subject. Applicants respectfully assert that there is no reason in Russell-Jones, Dean or the general knowledge in the art to combine these references. As mentioned above, since

somatostatin is a tetradecapeptide, it cannot be used to make an analog that would retain the necessary tertiary structure to induce autoantibodies. Therefore, rather than support the Examiner's argument, Dean actually teaches away from the combination of references. A prior art reference must be considered in its entirety, including portions that would lead away from the claimed invention. *See* M.P.E.P. § 2141.02(VI) (citing *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983)); *see also Panduit Corp. v. Dennison Mfg. Co.*, 774 F.2d 1082, 1093-94 (Fed. Cir. 1985) ("The well established rule of law is that each prior art reference must be evaluated as an entirety . . . ."). That is, "[t]here is no suggestion to combine . . . if a reference teaches away from its combination with another source." *Tec Air, Inc. v. Denso Manufacturing Michigan Inc.*, 192 F.3d 1353, 1360 (Fed. Cir. 1999); *see also KSR* at 12 (reaffirming "the corollary principle that when the prior art teaches away from combining certain known elements, discovery of a successful means of combining them is more likely to be nonobvious") (citing *United States v. Adams*, 383 U.S. 39, 51-52 (1966)). At best, Russell-Jones is an invitation to manipulate otherwise immunogenic molecules, and not to manipulate a self-protein, *which is non-immunogenic*, to cause production of autoantibodies when administered to a subject. As such, Russell-Jones in view of Dean does not render the claims obvious. Accordingly, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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